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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/603,406	06/24/2003	Pier Andrea Borea	PAT-0040-US-NP2	4184

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EXAMINER	
GEMBEH, SHIRLEY V	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
08/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/603,406	BOREA ET AL.	
	Examiner	Art Unit	
	Shirley V. Gembeh	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16,18-21 and 28-32* is/are pending in the application.

4a) Of the above claim(s) *1-5* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *6-16,18-21 and 28-32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

The response filed **10/6/06** presents remarks and arguments to the office action mailed **7/6/06**. Applicants' request for reconsideration of the rejection of claims in the last office action has been considered.

Applicants' arguments, filed, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Status of Action

Claims 6-16, 18-21 and 28-32 are examined.

Maintained Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9 and 20 remain rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written rejection requirement. There is no teaching in the instant application or prior art for the making of the claimed compounds wherein A is a triazolo ring as in the last office action of record.

Applicant argues that one skilled in the art would know how to make compounds of the claimed invention by following the teachings of WO/00/15231. Applicants' admission that the WO 00/15231 does not disclose specific examples of compounds of formula I wherein A is a triazolo ring (see page 9 of remarks) makes it difficult for one skilled in the art to make and use the claimed compound formula.

The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

If Applicant is relying on the WO 00/15231 document, then Applicant must follow the above proper incorporation method. The instant specification fails to indicate that a representative number of structurally related compounds are disclosed and therefore, the artisan would not know the identity of a reasonable number of representative compounds falling within the scope of the instant claim and would not know how to use them. Applicant's arguments have been fully considered but are not deemed persuasive.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 6-8, 10-16, 18-19, 21 and 28-32 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 6,210,917 to Carson et al. in view of Jacobson et al. US Patent No. 6,066,642 and further in view of Baraldi et al., Journal of Medicinal Chemistry. Vol. 42 (1999) 4473-4478 (all of record) and Goodman and Gilman, The pharmacological Basis of Therapeutics.

Carson et al. teach an adenosine-5'- triphosphate depleting agent to treat cancers such as breast and colon cancer (see col.12 lines 53-55) that are multidrug resistant, MDR, (see Abstract) in combination with chemotherapeutic agents. See col. 2, lines 37-40 and with respect to vinca alkaloids, taxanes and antibiotics, see col. 1

lines 46-51. Carson et al. additionally explain that the depletion of AMP and ATP negatively affects P-glycoprotein activity, which is linked to MDR.

Jacobson et al. teach the use of adenosine A3 receptor antagonists in the killing of cancer cells (in current claims 23-25; see col. 63 Example 31) wherein the A3 receptor antagonists are used alone or in combination with other active agents (see col. 16 lines 11-18).

Jacobson et al. do not specifically teach the use of a compound MRE3008F20 of the instant claims, for example.

Baraldi et al. teach MRE3008F20 is an adenosine A3 receptor antagonists (in current claims 23-25; see page 4476 compound #7).

Although, the use of the term synergism is not explicitly used, Goodman and Gilman teach the combination therapy, using a drug with known other anticancer agents. See pages 1225 and 1230 with asterisks.

The motivation to combine arises from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Section MPEP 2144.07

Applicant argues that the claimed invention was not obvious individually analyzing the references and that the Examiner's opinion that reduction in adenosine levels would be efficacious in the treatment of cancer is nowhere reported.

This is found nonpersuasive. Even, though Carson et al. do not teach synergism explicitly, combination therapy comprising an adenosine-5'-triphosphate- depleting

agent to treat cancers that are multidrug resistance is taught. See col. 2, lines 37-40. Jacobson et al. teach adenosine A3 receptor antagonists are used in combination with other active agents, motivating one of ordinary skill in the art to use other known chemotherapeutic agents for the purpose of treating cancer. Combination therapy with new drugs and existing drugs is well known in the art as taught by Goodman and Gilman (see enclosed document especially pages1225 and 1230 with astericks).

Further, to remedy the deficit drawn to the specific compound, Baraldi teaches MRE3008F20 is an adenosine A3 receptor antagonist, the specific A3 receptor antagonist claimed thus providing one of ordinary skill in the art motivation to combine the teachings of Jacobson. Applicants argue there is no suggestion to combine the references. The examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988) and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). Applicant's arguments have been fully considered but they are not persuasive. The rejection is maintained as in the last office action of record. However, The motivation to combine can arise from the expectation that the prior art elements will perform their expected functions to achieve their expected results when combined for their common known purpose. Section MPEP 2144.07

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shirley V. Gembeh whose telephone number is 571-272-8504. The examiner can normally be reached on 8:30 -5:00, Monday- Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

7/30/07
SVG

Phyllis Spivack

PHYLLIS SPIVACK
PRIMARY EXAMINER